

Gene Section

Mini Review

PTPN13 (Protein tyrosine phosphatase, non-receptor type 13)

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Identity

Other names: DKFZp686J1497; FAP-1; PNP1; PTP-BAS; PTP-BL; PTP-E1; PTP1E; PTPL1; PTPLE

HGNC (Hugo): PTPN13

Location: 4q21.3

Note: Genomic context: PTPN13 lies in a head-to-head conformation with MAPK10/JNK3 and they share a 633 bp bi-directional promoter which is a typical CpG island.

DNA/RNA

Description

The gene covers 220.87 kb (from 87734485 to 87955350-NCBI) and contains 48 exons and 51 different introns (49 gt-ag, 2 gc-ag), initiates transcription within exon 2 and terminates in exon 48.

Transcription

Transcription produces 13 different mRNAs, 9 alternatively spliced variants and 4 unspliced forms. RefSeq annotates 4 representative transcripts, but Homo sapiens cDNA sequences in GenBank support at least 9 spliced variants.

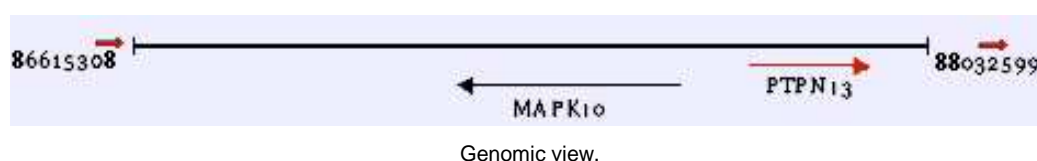
Protein

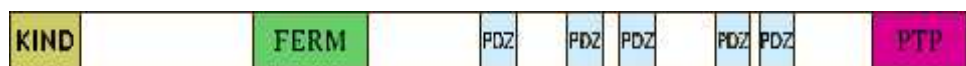
Description

The protein encoded by this gene is a member of the protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation. This PTP is a large protein that possesses a PTP domain at C-terminus, and multiple noncatalytic domains, which include a domain with similarity to band 4.1 superfamily of cytoskeletal-associated proteins, a region consisting of five PDZ domains, and a leucine zipper motif. This PTP was found to interact with, and dephosphorylate Fas receptor, as well as IkappaBalpha through the PDZ domains, which suggested its role in Fas mediated programmed cell death. This PTP was also shown to interact with GTPase-activating protein, and thus may function as a regulator of Rho signaling pathway. Eight spliced and the unspliced mRNAs putatively encode good proteins.

Expression

In all human normal tissues, including lymph node and peripheral blood mononuclear cells samples, PTPN13 is ubiquitously expressed.





Schematic representation of PTPN13 structure and boxes represent functional domains. The KIND domain has been identified in silico by sequence homology.

Localisation

The FERM domain binds to phosphatidylinositol 4,5-biphosphate leading to the enrichment of PTPN13 at a juxtamembrane localization. However, the PTPN13 protein is also detected throughout the cytoplasm. In HeLa cells, PTPN13 localizes to the centrosomes during metaphase.

Function

Functionally, the gene has been tested for association to diseases (bone neoplasms; carcinoma; colorectal neoplasms; liver neoplasms; lymphoma; sarcoma, Ewing's), proposed to participate in a pathway (FAS signaling pathway (CD95)) and a process (protein amino acid dephosphorylation). Proteins are expected to have molecular functions (non-membrane spanning protein tyrosine phosphatase activity, hydrolase activity, protein binding, structural molecule activity) and to localize in various compartments (nucleus, cytoplasm, cytoskeleton).

Mutations

Note

Different somatic mutations was identified in colorectal tumors (19% of the colorectal cancer

samples analyzed), predicted to result in missense or non-sense mutations. Some of these mutant proteins led to reduce phosphatase activity.

Implicated in

Colorectal cancers

Disease

A large-scale study that looked at the mutations in the tyrosine phosphatome from colorectal cancers identified PTPN13. The authors identified 19 mutations, non-sense and missense, seven of which were in the PTP domain.

Lymphomas (Hodgkin and non-Hodgkin), gastric and hepatocellular tumors

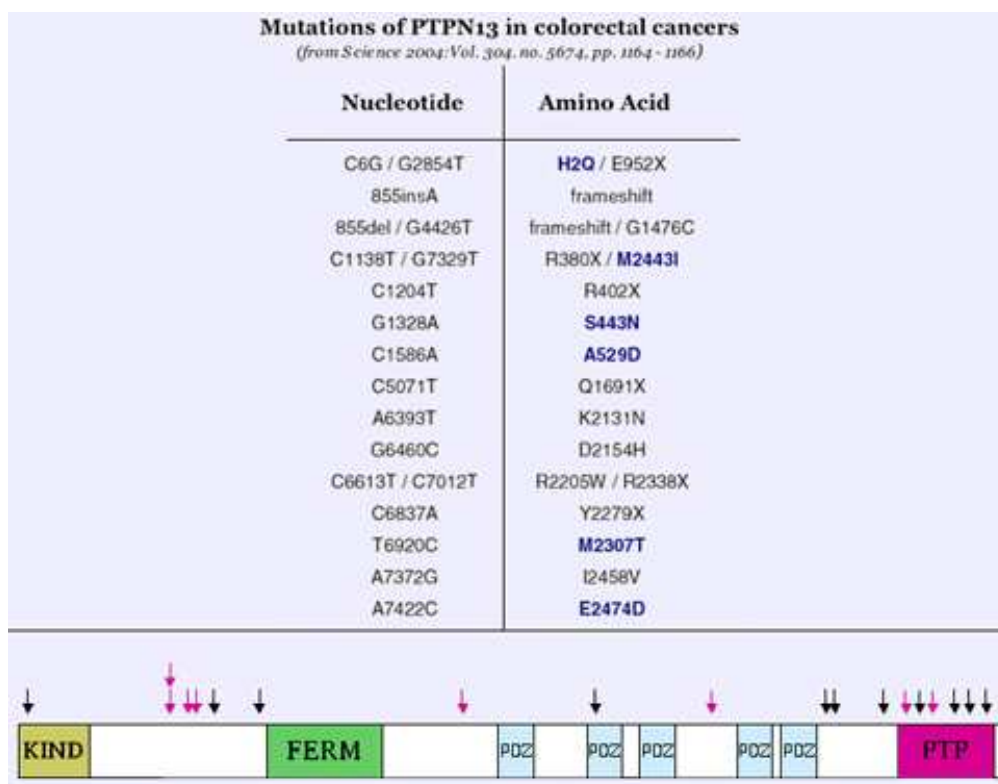
Disease

Hypermethylation of the PTPN13 promoter or allelic loss was observed leading to downregulation of PTPN13 mRNA.

To be noted

Note

Several evidences suggest that PTPN13 may act



Distribution of mutations in PTPN13, black arrows indicate location of missense mutations, red arrows indicate location of nonsense mutations or frameshifts.

differently as a tumor promoting gene depending upon the disease context. The modulation of Fas-mediated cell death by PTPN13 could enhance tumor growth by blocking death signaling.

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